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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/780,653	QASBA ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 6-8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: non-compliant amendment to the spec..

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on December 27, 2004 has been entered.

DETAILED ACTION

This application is a continuation of 09/316,797, filed May 21, 1999, which claims benefit to 60/086,420, filed May 22, 1998 and 60/108,308, filed November 13, 1998.

As requested Applicants' amendment filed July 12, 2004 has been entered. Claims 4 and 5 have been amended. Claims 1-8 are pending.

Election/Restriction

Applicant's election of group II, claims 4 and 5, in Paper No. 3, was acknowledged. It was noted that because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-8 are pending. Claims 1-3, 6-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Claims 4 and 5 are currently under examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

This application lacks the necessary reference to the prior application because a statement reading "This is a continuation of Application No. 09/316,797, filed May 21, 1999." should be entered following the title of the invention or as the first sentence of the specification. Also, the current status of all nonprovisional parent applications referenced should be included.

It is noted that Applicants have request that the specification be amended (see page 6), however this is not a proper means to amend the specification. See attached Notice of Non-Compliant Amendment (37CFR 1.121).

In addition, it is noted that if this is an application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four

months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly amended claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". The claims have been amended to recite "and purified" however literal support for this term can not be found in the present specification. Review of the entire specification finds support for "enriching" (page 6) and general means of isolating known in the art at the time of filing (methods of Haynesworth *et al.*, (1992) on page 12), however there is no specific description of a purified mesenchymal stem cell, nor the methods to provide such a purified cell wherein a mesenchymal stem cell is the only cell type in a composition.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 4 and 5 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described. As indicated above, there is no specific methodology set forth for providing a "purified" mesenchymal stem cell. Further, in light of the fact that there is no specific characteristics of the cell taught in the specification, it would be considered undue

experimentation to purify such a cell because it would require first a detailed characterization of the cell before the proper methods could even be established.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating a subject in need of megakaryocytes as platelet precursor cells comprising administering to said subject autologous or allogenic bone marrow in an amount effective to produce megakaryocytes, does not reasonably provide enablement for administering only mesenchymal stem cells or mesenchymal stem cells and CD34+ cells alone.

Applicants argue that it is not there burden to demonstrate that the claimed methods are effective, rather it is the burden of the Examiner to shoe the treatment would not be effective

(page 4). Noting the affect of mesenchymal stem cells on CD34+ cells acknowledged by the office, Applicants argue that there is no specific evidence that the claimed method would not work, other than speculation (page 4). Applicants argue that the present specification provides clear guidance to situations and conditions for patients that would benefit from the instantly claimed methods (page 4). Finally, Applicants argue that the breadth of using mesenchymal stem cells from any tissue beyond bone marrow is enabled because there is no objective evidence that cells from other tissues would not work (pages 4-5). It is noted that working examples are not required and that it would be routine for the skilled artisan to administer mesenchymal stem cells to a subject (page 5-6). See Applicants' amendment, pages 3-6. Applicants arguments have been fully considered, but not found persuasive.

As stated previously, 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). Further, the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). Finally, case law teaches (*Ex parte Forman*, 230 USPQ 546,547 (BPAI 1986)) that "the disclosure of a patent application must enable practice of the invention claimed without undue experimentation", wherein factors involved in the determination of undue experimentation were deemed to include "the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims." As set forth in the previous office action, there is no

working example nor guidance regarding the method of administration of mesenchymal cells on megakaryocytopoiesis *in vivo*. The specification does demonstrate that mesenchymal cells can affect CD34+ cells *in vitro*, however only refers generally to use of production of differentiated megakaryocytes (page 11, line 15), and does not disclose any guidance regarding administration or conditions to produce these affects *in vivo*. Thus the claimed invention is based on the speculation that observation made *in vitro* can be simply extended to method *in vivo*. In this case, lacking any specific examples in the art or the specification demonstrating the claimed invention is fully enabled, the Examiner must access that basis of the invention and whether simple *in vitro* experiments can be extended to working methods of treatment in a more complex *in vivo* system. It is noted that Applicants' do not specifically discuss or dispute the evidence provided in the cited references of Ellis *et al.*, Berenson *et al.*, Bertolini *et al.* or Emerson used in the basis of the rejection, only that Examiner relies on speculation. This argument is not found persuasive because sound scientific arguments based on cited references is provided by the Examiner. Moreover, the Examiner has set forth in the basis of the rejection each of Wands factors. Examiner acknowledges that the burden of proof lies first with the office, however in this case a *prima facie* case demonstrating limitations recognized in the art has been established and a review of the teaching of the specification has been done demonstrating that the teachings therein fail to adequately address the art recognized problems. It is noted and acknowledged that there is no specific statement in any of the cited references that practicing the claimed method would not work. However, each of the cited references provide specific limitations recognized in the art at the time of filing that would have to be overcome in order to practice the claimed invention in the full breadth as instantly claimed for both claims 4 and 5

As noted previously in the basis of the rejection, the specification is silent with respect to any disease or condition in which only megakaryocytes are required. Examiner would agree that claimed method if enabled could be practiced with other methods of treatment known in the art, however the specification does not provide any specific guidance to what these other treatments are or how they would be combined with the instantly claimed methods. Again, the reasons and/or circumstances of 'a patient in need of megakaryocytes' alone are not specifically discussed or defined in the specification or the art of record, which has bearing on the predictability of treating a patient in need thereof, because the effective amount to be administered can not be clearly assessed lacking any specific condition or disease to be treated. Thus, while claim 5 encompasses administering CD34+ cells which have the potential to differentiate into megakaryocytes, the specification lacks any guidance on how the cells would be administered, at what concentration for what diseases of conditions. Again there is no working example nor guidance regarding the method of administration of mesenchymal cells on megakaryocytopoiesis *in vivo*. The specification demonstrates that mesenchymal cells can affect CD34+ cells *in vitro*, and only refers generally to use of production of differentiated megakaryocytes (page 11, line 15), and does not disclose any guidance regarding administration or conditions to produce these affects *in vivo*.

The claimed methods comprises administering mesenchymal stem cells and relies on the ability to promote megakaryocyte differentiation of CD34+ cells as observed in *in vitro* studies. It was known in the art that the CD34+ hematopoietic stem cells are the cells in the bone marrow capable of differentiating and giving rise to multiple lineages including megakaryocytes. Thus, even if one were to treat individuals receiving chemotherapy, a bone marrow transplant or a

peripheral blood stem cell transplants none of these subjects contain the CD34+ hematopoietic stem cells which are necessary and capable of being induced and differentiating into megakaryocytes. Thus, claim 4 encompasses providing mesenchymal stem cells to a subject under conditions wherein the cells required, the CD34+ cells, are not present.

With respect to the delivery of any type mesenchymal stem cell, Examiner acknowledges that the claims do not encompass simply providing a mesenchymal cell. However, the specification clearly contemplates sources other than the bone marrow, though the preferred source is the bone marrow (page 6; line 12). To this end, the claims encompass the use of mesenchymal stem cells from other tissue sources. The specification provides no guidance to methods for isolating mesenchymal stem cells from other tissues, nor if such cells were isolated or exist, if they would possess the properties of mesenchymal stem cells isolated from the bone marrow. Examiner has cited Dexter *et al.* to demonstrate that 'cells from the spleen, liver, or other tissues do not support hemopoiesis *in vitro*' (page 432, first column). Clearly, if these cells sources can not support growth *in vitro*, there is little expectation that they would obtain new properties and support any growth *in vivo*. The physiological art in general is acknowledged to be unpredictable (MPEP 2146.03). To this end Examiner has cited Emerson who reviews the success of expanded bone marrow cultures ability to recover megakaryocytopoiesis in patients (page 3085; section on INITIAL CLINICAL EXPERIENCE...), and described the successful engraftment of *ex vivo* expanded CD34+ cells (last paragraph). However, all the methods described to restore megakaryocytopoiesis *in vivo* have relied on administration of a "stem cell" or "progenitor cell" which is capable of differentiating into the desired cell type, and to date, there is no report that administration of a

"mesenchymal cell" would produce the same effect as a "stem cell" upon administration. The specification does not demonstrate nor disclose prior art demonstrating that differentiation effects of isolated mesenchymal cells can occur *in vivo* when administered to a patient. With respect to claim 4 applicant makes the supposition that a stem cell capable of producing a megakaryocyte is present *in vivo*, and with respect to claim 5, that administration of both mesenchymal supporting and stem cell would allow for megakaryocytopoiesis.

In addition, beyond the general teaching of the specification for deficiencies of megakaryocytes in a subject, the art teaches that the presence of low amounts of megakaryocytes can be due to physiological conditions as is found in thrombocytopenia, megaloblastic anemia, or in a patient who is deficient in folate or Cbl where maturation of megakaryocytes can be disrupted (Handin *et al.*, pages 1399-1401). In these instances, the lack of megakaryocytes is due to an inhibition of differentiation of CD34+ hematopoietic stem cells. Therefore, a method of treatment as stated in claims 4 or 5 would not produce megakaryocytes in such a patient in need of megakaryocytes because the claimed method does not remedy nor address the fundamental physiological problem in these types of subjects. Again, subjects contemplated by the specification as needing megakaryocytes are patients in which most or all of the hematopoietic system has been impaired or destroyed. Therefore, these patients lack hematopoietic stem cells which are capable of differentiating into megakaryocytes. In these patients administering mesenchymal stem cells will have no affect on megakaryocyte formation because the required cell types mesenchymal stem cells could potentially affect are not even present. The specification is silent to discussion of any other conditions requiring

megakaryocytes, and in view of the art, the physiologically basis of these disorders would indicate that the claimed methods would not remedy their fundamental deficiencies.

Not addressed by Applicants amendment is the issue that the claims are not limited to administering autologous or allogenic mesenchymal stem cells, and broadly encompass xenogeneic cell transplantation which to date has not been successfully performed for any form of treatment. The specification specifically contemplates using non-matched donor cells (page 6, lines 4-6), and therefore encompasses transplantation of cells to a subject from an unrelated species. In both cases the specification is silent with respect to any discussion or guidance to overcome these long time art recognized limitations. It is noted that Applicants have not addressed this specific issue in the traversal and have not amended the claims accordingly.

Enablement has been considered in view of the Wands factors (MPEP 2164.01(a)). The factors considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In view of the of the lack of guidance, working examples, breadth of the claims, skill in the art and state of the art at the time of the claimed invention, it would require undue experimentation by one of skill to practice the invention as claimed.
The prior art demonstrates that megakaryocyte development is a complex, multi-step process dependent on numerous positive and negative affecters as well as specific cell-cell interaction (page 1, summary of thromboiesis by Ellis *et al.*) It is noted that differentiation of progenitor cells into megakaryocytes *in vitro* has be achieved using various culturing conditions and

addition of growth/stimulating factors to the media, and that explant of bone marrow, in particular the CD34+ hematopoietic stem cells in the marrow are capable of differentiating into megakaryocytes *in vivo*. Applicants have defined a potential use of an *in vivo* method of treatment using mesenchymal cells, but essentially have left all of the work required to develop a working method *in vivo* for any patient in need of megakaryocytes has been left to others. The specification fails to provide the necessary guidance to overcome art recognized limitations encompassed by the breadth of the claims and fails to provide a nexus from observations made in an *in vitro* culture system to an *in vivo* method of treatment of a patient.

Therefore, for the reasons above and of record, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claims have been amended to recite "purified" however this term is not defined in the specification. Purified is a relative term, and can encompass anything from taking it from the original source to obtaining a composition having solely one product. The claims are indefinite because the metes and bounds of purified is not clearly set forth in the claims nor the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4 and 5 stand rejected under 35 U.S.C. 102(b) as being anticipated by Lemoli *et al.* (Acta Haematologica 95:164-170, (1996)) as evidenced in Developmental Biology (page 357).

Applicants summarize the invention and the teaching of Lemoli *et al.* and argue that Lemoli *et al.* does not disclose the isolation and purification of mesnechymal stem cells or the administration of isolated mesenchymal stem cells to a patient. See Applicants' amendment , Section C, page 3. Applicants' arguments have been fully considered but not found persuasive.

As indicated above and in the advisory action, the term purified is a relative term and can reasonably be interpreted to encompass taking a sample from its original source. In this case Lemoli *et al.* teaches this limitation. Like the term "isolated" each is a broad general term encompassing the removal of sample from a location it is normally found. Applicants arguments that the claimed invention is differentiated from that disclosed in the art appears to focus on the use of a 'purified' preparation of mesenchymal stem cells. In the instant case the removal of bone marrow from an individual containing mesenchymal stem cells would be considered 'isolated' from the subject. Applicants arguments are not found persuasive because Lemoli *et al.* teach the administration of isolated samples, in particular the adminstration of bone marrow isolated from a subject. Applicants do not contest the fact that mesenchymal stem cells

are found in bone marrow, therefore the isolated bone marrow samples containing mesenchymal stem cells anticipates the claims as instantly amended. As noted in the basis of the previous rejection, with respect to the single method step recited in the claims, the administration of mesenchymal stem cells (claim 4) and the administration of mesenchymal stem cells and CD34+ cells is broad encompassing any means of delivery and the delivery of the cells in any composition. The specification contemplates **any** process of obtaining mesenchymal stem cells or co-recovery of hematopoietic progenitor cells and mesenchymal stem cells (page 6, lines 18-24) which could subsequently be used in the claimed methods. The specification teaches that a preferred source of mesenchymal stem cells is the bone marrow (page 6, lines 11-12). Accordingly, a reasonable interpretation of the instant claims in light of the guidance of the instant specification is a method comprising administering bone marrow to a subject who has undergone radiation therapy wherein said therapy ablates the cells of the hematopoietic system. Again, the claims are directed to providing megakaryocytes to a patient in need thereof, and while the specification is silent with respect to any specific condition wherein only megakaryocytes are required, it teaches generally that a subject in need of platelets, such as individuals receiving chemotherapy or bone marrow transplant, would benefit from the instantly claimed method (page 8, lines 8-12).

As set forth in the basis of the final rejection, Lemoli *et al.* teach a method of autologous bone marrow transplantation to patients undergoing myeloablative chemotherapy (page 165, Study Design section). Specifically, bone marrow was removed from the patient before chemotherapeutic treatment (page 165, BM samples section). Analysis of the patients after myeloablative treatment and delivery of the autologous bone marrow indicated that an increase

in platelets could be detected (summarized in figure 2, lower graph). Lemoli et al. does not specifically characterize or state that megakaryocytes are produced by this procedure, however the formation of platelets, the end product of megakaryocyte differentiation, is a clear indication that megakaryocytes are formed in the subject (see figure 9.39 on page 357 in Developmental Biology as evidence of megakaryocyte differentiation pathway). Thus, the development of platelets indicates that sufficient amounts cells were administered to affect the patient. In this case, in light of the teaching and guidance of the specification the limitations of an autologous bone marrow transplant to patients who have undergone chemotherapeutic treatment, and the evidence of recovery of platelet formation in said patients after the administration of bone marrow anticipates the instantly claimed methods. As noted in the previous office action, the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Woitach

Joe Woitach
AU1632

UNITED STATES PATENT AND TRADEMARK OFFICE

UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AN
DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFIC
WASHINGTON, DC 202
www.uspto.go

Paper No.

Notice of Non-Compliant Amendment (37 CFR 1.121)

The amendment document filed on 7/11/04 is considered non-compliant because it has failed to meet the requirements of 37 CFR 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). In order for the amendment document to be compliant, correction of the following omission(s) or provision is required. **Only the section (1.121(h)) of the amendment document containing the omission or non-compliant provision must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment document must be re-submitted.**

THE FOLLOWING CHECKED (X) ELEMENTS(S) CAUSE THE AMENDMENT DOCUMENT TO BE NON-COMPLIANT:

☒ 1. Amendments to the specification:
- ☒ A. Amended paragraph(s) do not include markings.
- ☐ B. New paragraph(s) should not be underlined.
- ☒ C. Other not on separate sheets.

☐ 2. Abstract:
- ☐ A. Not presented on a separate sheet. 37 CFR 1.72.
- ☐ B. Other_____

☐ 3. Amendments to the drawings: _____

☐ 4. Amendments to the claims:
- ☐ A. A complete listing of all of the claims is not present.
- ☐ B. The listing of claims does not include the text of all claims (incl. withdrawn claims)
- ☐ C. Each claim has not been provided with the proper status identifier, and as such, the individual status of each claim cannot be identified.
- ☐ D. The claims of this amendment paper have not been presented in ascending numerical order.
- ☐ E. Other: _____

For further explanation of the amendment format required by 37 CFR 1.121, see MPEP Sec. 714 and the USPTO website at http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/officeflyer.pdf.

If the non-compliant amendment is a **PRELIMINARY AMENDMENT,** applicant is given ONE MONTH from the mail date of this letter to supply the corrected section which complies with 37 CFR 1.121. Failure to comply with 37 CFR 1.121 will result in non-entry of the preliminary amendment and examination on the merits will commence without consideration of the proposed changes in the preliminary amendment(s). This notice is not an action under 35 U.S.C. 132, and **this ONE MONTH time limit is not extendable.**

If the non-compliant amendment is a reply to a **NON-FINAL OFFICE ACTION,** and since the amendment appears to be a *bona fide* attempt to be a reply (37 CFR 1.135(c)), applicant is given a TIME PERIOD of ONE MONTH from the mailing of this notice within which to re-submit the corrected section which complies with 37 CFR 1.121 in order to avoid abandonment. **EXTENSIONS OF THIS TIME PERIOD ARE AVAILABLE UNDER 37 CFR 1.136(a).**

If the amendment is a reply to a **FINAL REJECTION,** this form may be an attachment to an Advisory Action. **The period for response to a final rejection continues to run from the date set in the final rejection**, and is not affected by the non-compliant status of the amendment.

Legal Instruments Examiner (LIE) Joe Walters

July 22, 2003 (rev.)